



JACC

SEPTEMBER 28, 2010
VOLUME 56, No. 14

**QUARTERLY FOCUS ISSUE:
PREVENTION/OUTCOMES**



JOURNAL of the AMERICAN COLLEGE of CARDIOLOGY

Inside This Issue

STATE-OF-THE-ART PAPER

Troponin Elevation in Patients With Heart Failure

1071

Robb D. Kociol, Peter S. Pang, Mihai Gheorghiade, Gregg C. Fonarow, Christopher M. O'Connor, G. Michael Felker

Natriuretic peptides have become increasingly important for the diagnosis and risk stratification of patients with heart failure (HF). Many patients with HF also have detectable levels of circulating cardiac troponin (cTn). Kociol and colleagues review the implications of measuring and detecting cTn with the knowledge that more sensitive cTn assays are being developed that can reliably quantify cTn at much lower levels. While the exact mechanism of troponin release is unknown, research suggests that it may be related to myocyte necrosis, apoptosis, or cTn degradation or release in otherwise viable cells; each of these processes would lead to worsening cardiac dysfunction over time. Measuring cTn may help to clarify the mechanism of worsening HF, improve risk stratification, and aid in the early detection of harmful side effects of new therapies.

EARLY PHASE CLINICAL TRIALS

sPLA₂ Inhibitor Reduces Inflammatory Biomarkers in Post-ACS Subjects

1079

Robert S. Rosenson, Colin Hislop, Michael Elliott, Yuri Stasiv, Michael Goulder, David Waters

Varespladib, a selective secretory phospholipase A₂ (sPLA₂) inhibitor, has been shown to lower levels of sPLA₂-IIA by more than 90%, low-density lipoprotein cholesterol (LDL-C) by 12% to 18%, and high-sensitivity C-reactive protein (hsCRP) by 20% to 40% in stable coronary heart disease patients. This randomized controlled trial investigated the effects of sPLA₂ inhibition with varespladib as adjunctive therapy to atorvastatin in patients with recent acute coronary syndrome (ACS). After 8 weeks, varespladib/atorvastatin reduced mean LDL-C levels from baseline by 50% compared to 43% with placebo/atorvastatin, with reductions in sPLA₂-IIA levels of 82% and 16%, and nonsignificant differences in hsCRP reductions. The rate of major adverse cardiovascular events was not different from placebo after 6 months in the small trial, and there were no safety problems identified. Varespladib safely reduces LDL-C and sPLA₂-IIA in post-ACS patients, but larger studies are needed to determine its effect on outcomes.

(continued on page A-20)

EARLY PHASE CLINICAL TRIALS

Implanted Monitor Can Detect Coronary Ischemia**1089**

Tim A. Fischell, David R. Fischell, Alvaro Avezum, M. Sasha John, David Holmes, Malcolm Foster III, Richard Kovach, Paulo Medeiros, Leopoldo Piegas, Helio Guimaraes, C. Michael Gibson

Fischell and colleagues report the first clinical studies of intracardiac ST-segment monitoring in ambulatory humans to detect coronary ischemia. The device uses a modified lead implanted into the right ventricular apex, which is implanted in a manner similar to a pacemaker. It is programmed to the patient's baseline levels of ischemia. For ST-segment changes beyond the thresholds, the device emits an audible alarm. During follow-up of 37 subjects, 4 developed ST-segment shifts >3 SDs of their normal daily range. This prompted emergent evaluations that confirmed coronary occlusion or ruptured plaque, with a median alarm-to-door time of 19.5 min. The device also detected progressive atherosclerosis in the form of demand-related ischemia in 4 other subjects.

CARDIAC INTERVENTION AND SURGERY

Meta-Analysis Confirms Benefit of Pre-Procedural Statin Therapy**1099**

David E. Winchester, Xuerong Wen, Lola Xie, Anthony A. Bavry

Winchester and colleagues performed a meta-analysis of trials that randomized subjects to statins prior to percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), or noncardiac surgery. Pre-procedural statins significantly reduced post-procedural myocardial infarction (MI) (risk ratio [RR]: 0.57) in the almost 5,000 subjects. This benefit was seen after both PCI and noncardiac surgical procedures, but not after CABG. All-cause mortality was nonsignificantly reduced from statin therapy (RR: 0.66, $p = 0.15$). Pre-procedural statins also reduced post-CABG atrial fibrillation. Statins administered before invasive procedures significantly reduce the risk of post-procedural MI, with favorable trends for mortality.

Editorial Comment: Kim A. Eagle, Vineet Chopra, p. 1110

METABOLIC SYNDROME

Meta-Analysis Confirms Increased Risk in Patients With Metabolic Syndrome**1113**

Salvatore Mottillo, Kristian B. Filion, Jacques Genest, Lawrence Joseph, Louise Pilote, Paul Poirier, Stéphane Rinfret, Ernesto L. Schiffrin, Mark J. Eisenberg

Mottillo and colleagues conducted a systematic review and meta-analysis of the cardiovascular risk associated with the metabolic syndrome as defined by the 2001 National Cholesterol Education Program and the 2004 revised National Cholesterol Education Program definitions. A total of 87 studies were identified, which included almost 1 million subjects. The metabolic syndrome was associated with an approximate doubling in the risk of each of the following end points: cardiovascular disease (CVD), CVD mortality, all-cause mortality, myocardial infarction, and stroke. These results confirm that the metabolic syndrome is associated with increased cardiovascular risk.

HEART RHYTHM DISORDERS

Fewer Procedural Complications in Hospitals That Implant More ICDs

1133

James V. Freeman, Yongfei Wang, Jeptba P. Curtis, Paul A. Heidenreich, Mark A. Hlatky

Freeman and colleagues examined the relationship between hospital implantable cardioverter-defibrillator (ICD) implantation volume and procedural complications using data from the National Cardiovascular Data Registry ICD Registry. The rate of adverse events declined progressively with increasing procedure volume and remained significant after adjustment for patient clinical, operator, and hospital characteristics. Patients who have an ICD implanted at a high-volume hospital are less likely to have an adverse event associated with the procedure than patients who have an ICD implanted at a low-volume hospital.

HEART FAILURE

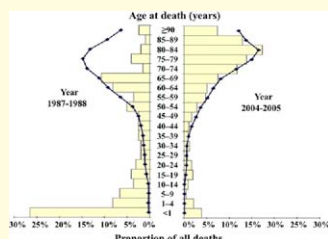
Physical Activity Linked to Decreased Risk of HF

1140

Yujie Wang, Jaakko Tuomilehto, Pekka Jousilampi, Riitta Antikainen, Markku Mähönen, Peter T. Katzmarzyk, Gang Hu

Wang and colleagues studied whether occupational, commuting, or leisure-time physical activity reduced the risk of heart failure (HF). Nearly 60,000 Finnish men and women were asked about different kinds of physical activity along with other potential predictors of HF and were then followed for a mean of 18 years. After adjustment, active occupational activity reduced the risk of HF by 10% to 20%, with stronger reductions for high leisure-time physical activity. There were further reductions when subjects were active in more than one domain. Moderate and high levels of physical activity may reduce the risk of HF.

CONGENITAL HEART DISEASE



CONGENITAL HEART DISEASE

Decreasing Childhood Deaths in Patients With Congenital Heart Disease

1149

Paul Khairy, Raluca Ionescu-Ittu, Andrew S. Mackie, Michal Abrahamowicz, Louise Pilote, Ariane J. Marelli

Khairy and colleagues performed a population-based cohort study of patients with congenital heart disease (CHD) to determine if recent advances have altered rates of mortality. Between 1987 and 2005, almost 72,000 people were identified as having CHD and were followed for nearly 1 million patient-years. The proportion of infant and childhood deaths markedly declined from 1987 to 2005. Mortality rates decreased in all age groups below 65 years, with the largest reduction in infants (mortality rate ratio: 0.23). Deaths in patients with CHD have shifted away from infants toward adults, with a steady increase in age at death.